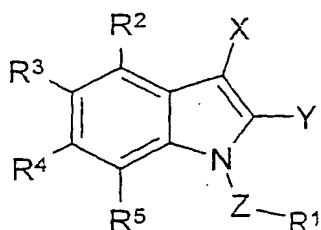


Claims

1. A compound of formula I,



5

wherein X represents an optionally substituted aryl or heteroaryl group or an optionally substituted amide, amine or sulfonamide group, which latter three groups are connected to the indole ring through their nitrogen atom;

10

Y represents a carboxylic acid, a carboxylic acid ester, a carboxylic acid amide, a hydroxamic acid, a hydroxamic acid ester or hydroxymethyl;

Z represents a spacer group;

15

R¹ represents an optionally substituted aryl or heteroaryl group;

one of the groups R², R³, R⁴ and R⁵ represents an optionally substituted aryl or heteroaryl group.

20

2. A compound as claimed in Claim 1; wherein:

X represents:

- i) an aryl group or a heteroaryl group, both of which groups are optionally substituted by one or more substituents selected from A; or
- 25 ii) -N(R⁶)-E-R⁷;

E represents a single bond, $-C(O)-$ or $-S(O)_n-$;

Y represents $-CH_2OH$, $-C(O)N(H)R^8$, $-C(O)N(H)OR^8$ or $-C(O)OR^8$;

5

Z represents a C_{1-8} alkylene or a C_{2-8} heteroalkylene chain, both of which:

- (i) optionally contain one or more unsaturations;
- (ii) are optionally substituted by one or more substituents selected from halo, $-R^8$, $-N(R^8)(R^9)$, $-OR^8$ and $=O$; and/or

10 (iii) may form part of an additional 3- to 8-membered ring formed between any one or more members of the C_{1-8} alkylene or C_{2-8} heteroalkylene chain, which ring optionally contains 1 to 3 heteroatoms and/or 1 to 3 unsaturations and which ring is itself optionally substituted by one or more substituents selected from halo, $-R^8$, $-N(R^8)(R^9)$, $-OR^8$ and $=O$;

15

R^1 represents an aryl or a heteroaryl group, both of which are optionally substituted by one or more substituents selected from A;

20 one of the groups R^2 , R^3 , R^4 and R^5 represents an aryl group or a heteroaryl group (both of which are optionally substituted by one or more substituents selected from A) and:

- a) the other groups are independently selected from hydrogen, G^1 , an aryl group, a heteroaryl group (which latter two groups are optionally substituted by one or more substituents selected from A), C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl or C_{3-8} heterocycloalkyl (which latter five groups are optionally substituted by one or more substituents selected from G^1 and/or Q^1); and/or
- b) any two other groups which are adjacent to each other are optionally linked to form, along with two atoms of the essential benzene ring in the compound of formula I, a 5- to 6-membered ring, optionally containing 1 or

more heteroatoms and/or 1 to 3 unsaturations, which ring is itself optionally substituted by one or more substituents selected from halo, -R⁸, -OR⁸ and =O;

5 A represents, on each occasion when mentioned above:

- I) an aryl group or a heteroaryl group, both of which are optionally substituted by one or more substituents selected from B;
- II) a C₁₋₆ alkyl, C₃₋₁₀ cycloalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl or C₃₋₈ heterocycloalkyl group, all of which are optionally substituted by one or 10 more substituents selected from G¹ and/or Q¹; or
- III) a G¹ group; or
- IV) two adjacent A substituents may be linked together to form, along with the essential atoms of the aryl or heteroaryl group to which the two A substituents are attached, a further 5- to 6-membered ring, optionally containing 1 or more heteroatoms and/or 1 to 3 unsaturations, which ring is 15 itself optionally substituted by one or more substituents selected from halo, -R⁸, -OR⁸ and =O;

G¹ represents, on each occasion when mentioned above, halo, cyano, -N₃, 20 -NO₂, -ONO₂ or -A¹-R¹⁰;

wherein A¹ represents a single bond or a spacer group selected from -C(Q²)A²-, -S(O)_nA³-, -N(R¹¹)A⁴-, -OA⁵- and -S-, in which:

A² represents A⁶ or -S-;

A³ represents A⁶;

25 A⁴ represents A⁷, -C(Q²)N(R¹¹)C(Q²)N(R¹¹)-, -C(Q²)N(R¹¹)C(Q²)O-, -C(Q²)N(R¹¹)S(O)_nN(R¹¹)-, -C(Q²)S-, -S(O)_nN(R¹¹)C(Q²)N(R¹¹)-, -S(O)_nN(R¹¹)C(Q²)O-, -S(O)_nN(R¹¹)S(O)_nN(R¹¹)- or -S(O)_nO-;

A⁵ represents A⁷ or -S(O)_nO-;

A⁶ represents a single bond, -N(R¹¹)- or -O-;

A⁷ represents a single bond, -C(Q²)-, -C(Q²)N(R¹¹)-, -C(Q²)O-, -S(O)_n- or -S(O)_nN(R¹¹);

Q¹ and Q² independently represent, on each occasion when mentioned above, =O, =S, =NR¹⁰, =NN(R¹⁰)(R¹¹), =NOR¹⁰, =NS(O)₂N(R¹⁰)(R¹¹), =NCN, =C(H)NO₂ or =C(R¹⁰)(R¹¹);

R⁶ and R⁷ independently represent, on each occasion when mentioned above:

10 I) hydrogen;
II) an aryl group or a heteroaryl group, both of which are optionally substituted by one or more substituents selected from B; or
III) a C₁₋₆ alkyl, C₃₋₁₀ cycloalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl or C₃₋₈ heterocycloalkyl group, all of which groups are optionally substituted by
15 one or more substituents selected from G² and/or Q³; or

R⁶ and R⁷ may be linked together to form along with the N atom and -E- group to which R⁶ and R⁷ are respectively attached, a 5- to 8-membered ring, optionally containing 1 to 3 heteroatoms and/or 1 to 3 unsaturations, which ring is optionally substituted by one or more substituents selected
20 from G² and/or Q³;

B represents, on each occasion when mentioned above:

I) an aryl group or a heteroaryl group, both of which are optionally substituted by one or more substituents selected from G² and/or wherein any
25 two adjacent atoms of the aryl or heteroaryl group may be linked together to form a further 5- to 6-membered ring, optionally containing 1 or more heteroatoms and/or 1 to 3 unsaturations, which ring is itself optionally substituted by one or more substituents selected from halo, -R⁸, -OR⁸ and =O;

II) a C_{1-6} alkyl, C_{5-10} cycloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl or C_{3-8} heterocycloalkyl group, all of which are optionally substituted by one or more substituents selected from G^2 and/or Q^3 ; or

III) a G^2 group; or

IV) two adjacent B substituents may be linked together to form, along with the essential atoms of the aryl or heteroaryl group to which the two B substituents are attached, a further 5- to 6-membered ring, optionally containing 1 or more heteroatoms and/or 1 to 3 unsaturations, which ring is itself optionally substituted by one or more substituents selected from halo, - R^8 , - OR^8 and =O;

G^2 represents, on each occasion when mentioned above, halo, cyano, - N_3 , - NO_2 , - ONO_2 or - A^8-R^{12} ;
 wherein A^8 represents a single bond or a spacer group selected from
 $-C(Q^4)A^9-$, - $S(O)_nA^{10}-$, - $N(R^{13})A^{11}-$, - $OA^{12}-$ and -S-, in which:
 A^9 represents A^{13} or -S-;
 A^{10} represents A^{13} ;
 A^{11} represents A^{14} , - $C(Q^4)N(R^{13})C(Q^4)N(R^{13})-$, - $C(Q^4)N(R^{13})C(Q^4)O-$, - $C(Q^4)N(R^{13})S(O)_nN(R^{13})-$, - $C(Q^4)S-$, - $S(O)_nN(R^{13})C(Q^4)N(R^{13})-$, - $S(O)_nN(R^{13})C(Q^4)O-$, - $S(O)_nN(R^{13})S(O)_nN(R^{13})-$ or - $S(O)_nO-$;
 A^{12} represents A^{14} or - $S(O)_nO-$;
 A^{13} represents a single bond, - $N(R^{13})-$ or - $O-$;
 A^{14} represents a single bond, - $C(Q^4)-$, - $C(Q^4)N(R^{13})-$, - $C(Q^4)O-$, - $S(O)_n-$ or - $S(O)_nN(R^{13})$;

25

Q^3 and Q^4 independently represent, on each occasion when mentioned above, =O, =S, =NR¹², =NN(R¹²)(R¹³), =NOR¹², =NS(O)₂N(R¹²)(R¹³), =NCN, =C(H)NO₂ or =C(R¹²)(R¹³);

30 $R^8, R^9, R^{10}, R^{11}, R^{12}$ and R^{13} are independently selected from:

- i) hydrogen;
- ii) an aryl or a heteroaryl group, both of which are optionally substituted by one or more substituents selected from G³ and/or wherein any two adjacent atoms of the aryl or heteroaryl group may be linked together to form a further 5- to 6-membered ring, optionally containing 1 or more heteroatoms, which ring is itself optionally substituted by one or more substituents selected from halo, -R¹⁴, -OR¹⁴ and =O; or
- iii) a C₁₋₆ alkyl, C₃₋₁₀ cycloalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl or C₃₋₈ heterocycloalkyl group, all of which are optionally substituted by one or more substituents selected from G³ and/or W¹; or
any pair of R⁸, R⁹, R¹⁰, R¹¹, R¹² and R¹³ may, for example when present on the same or on adjacent atoms, be linked together to form with those, or other relevant, atoms, a further 5- to 8-membered ring, optionally containing 1 to 3 heteroatoms and/or 1 to 3 unsaturations, which ring is itself optionally substituted by one or more substituents selected from G³ and/or W¹;

G³ represents, on each occasion when mentioned above, halo, cyano, -N₃, -NO₂, -ONO₂ or -A¹⁵-R¹⁵;

wherein A¹⁵ represents a single bond or a spacer group selected from -C(W²)A¹⁶-, -S(O)_nA¹⁷-, -N(R¹⁶)A¹⁸-, -OA¹⁹- and -S-, in which:

A¹⁶ represents A²⁰ or -S-;

A¹⁷ represents A²⁰;

A¹⁸ represents A²¹, -C(W²)N(R¹⁶)C(W²)N(R¹⁶)-, -C(W²)N(R¹⁶)C(W²)O-,

-C(W²)N(R¹⁶)S(O)_nN(R¹⁶)-, -C(W²)S-, -S(O)_nN(R¹⁶)C(W²)N(R¹⁶)-, -S(O)_nN(R¹⁶)C(W²)O-, -S(O)_nN(R¹⁶)S(O)_nN(R¹⁶)- or -S(O)_nO-;

A¹⁹ represents A²¹ or -S(O)_nO-;

A²⁰ represents a single bond, -N(R¹⁶)- or -O-;

A²¹ represents a single bond, -C(W²)-, -C(W²)N(R¹⁶)-, -C(W²)O-, -S(O)_n- or -S(O)_nN(R¹⁶);

W^1 and W^2 independently represent, on each occasion when mentioned above, $=O$, $=S$, $=NR^{15}$, $=NN(R^{15})(R^{16})$, $=NOR^{15}$, $=NS(O)_2N(R^{15})(R^{16})$, $=NCN$, $=C(H)NO_2$ or $=C(R^{15})(R^{16})$;

5

R^{14} , R^{15} and R^{16} are independently selected from:

- i) hydrogen;
- ii) an aryl or a heteroaryl group, both of which are optionally substituted by one or more substituents selected from G^4 , methylenedioxy, difluoromethylenedioxy and/or dimethylmethylenedioxy; or

10 iii) a C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl or C_{3-8} heterocycloalkyl group, all of which are optionally substituted by one or more substituents selected from G^4 and/or J ; or

15 any pair of R^{14} , R^{15} and R^{16} may, for example when present on the same or on adjacent atoms, be linked together to form with those, or other relevant, atoms, a further 5- to 7-membered ring, optionally containing 1 to 3 heteroatoms and/or 1 to 3 unsaturations, which ring is itself optionally substituted by one or more substituents selected from G^4 and J ;

20 G^4 represents, on each occasion when mentioned above, halo, cyano, $-N_3$, $-NO_2$, $-ONO_2$ or $-A^{22}-R^{17}$;

wherein A^{22} represents a single bond or a spacer group selected from $-C(O)A^{23}-$, $-S(O)_nA^{24}-$, $-N(R^{18})A^{25}-$, $-OA^{26}-$ and $-S-$, in which:

A^{23} represents A^{27} or $-S-$;

25 A^{24} represents A^{27} ;

A^{25} represents A^{28} , $-C(O)N(R^{18})C(O)N(R^{18})-$, $-C(O)N(R^{18})C(O)O-$, $-C(O)N(R^{18})S(O)_nN(R^{18})-$, $-C(O)S-$, $-S(O)_nN(R^{18})C(O)N(R^{18})-$, $-S(O)_nN(R^{18})C(O)O-$, $-S(O)_nN(R^{18})S(O)_nN(R^{18})-$ or $-S(O)_nO-$;

A^{26} represents A^{28} or $-S(O)_nO-$;

30 A^{27} represents a single bond, $-N(R^{18})-$ or $-O-$;

120

A²⁸ represents a single bond, -C(O)-, -C(O)N(R¹⁸)-, -C(O)O-, -S(O)_n- or -S(O)_nN(R¹⁸);

J represents, on each occasion when mentioned above, =O, =S, =NR¹⁷,
5 =NN(R¹⁷)(R¹⁸), =NOR¹⁷, =NS(O)₂N(R¹⁷)(R¹⁸), =NCN, =C(H)NO₂ or
=C(R¹⁷)(R¹⁸);

R¹⁷ and R¹⁸ are independently selected from hydrogen and C₁₋₆ alkyl, which latter group is optionally substituted by one or more substituents selected
10 from halo, -NH₂, -N(H)Me, -N(H)Et, -N(H)i-Pr, -NMe₂, -N(Me)Et,
-N(Me)i-Pr, -NET₂, -OH, -OMe, -OEt, -O*i*-Pr and =O; and

n represents, on each occasion when mentioned above, 1 or 2,

15 or a pharmaceutically-acceptable salt thereof.

3. A compound as claimed in Claim 2, wherein n represents 2.

4. A compound as claimed in Claim 2 or Claim 3, wherein A represents
20 G¹ or any two adjacent A substituents may be linked by a methylenedioxy group.

5. A compound as claimed in any one of Claims 2 to 4, wherein G¹ represents halo, cyano, -NO₂ or -A¹-R¹⁰.

25

6. A compound as claimed in any one of Claims 2 to 5, wherein A² represents A⁶.

7. A compound as claimed in any one of Claims 2 to 6, wherein A³ and
30 A⁵ independently represent a single bond.

8. A compound as claimed in any one of Claims 2 to 7, wherein A^4 represents a single bond, $-C(Q^2)-$ or $-S(O)_2-$.

5 9. A compound as claimed in any one of Claims 2 to 8, wherein Q^2 represents $=O$.

10. A compound as claimed in any one of Claims 2 to 9, wherein B represents G^2 .

11. A compound as claimed in any one of Claims 2 to 10, wherein G^2 represents halo, cyano, $-NO_2$ or $-A^8-R^{12}$.

12. A compound as claimed in any one of Claims 2 to 11, wherein A^8 represents a single bond, $-N(R^{13})A^{11}-$ or $-OA^{12}-$.

13. A compound as claimed in any one of Claims 2 to 12, wherein A^{11} and A^{12} independently represent a single bond.

20 14. A compound as claimed in any one of the preceding claims, wherein Z represents C_{1-6} alkylene, in which one of the carbon atoms in the chain may be replaced with oxygen.

25 15. A compound as claimed in any one of the preceding claims, wherein Y represents $-CH_2OH$, $-C(O)NHR^8$ or $-C(O)OR^8$.

16. A compound as claimed in any one of the preceding claims, wherein R^1 represents optionally substituted fluorenyl, phenyl or pyridyl.

17. A compound as claimed in any one of the preceding claims, wherein (when X represents an optionally substituted aryl or heteroaryl group) X represents an optionally substituted phenyl, thienyl, pyridyl, pyrazolyl, pyrazinyl or quinolinyl group.

5

18. A compound as claimed in any one of the preceding claims, wherein (when they represent an optionally substituted aryl or heteroaryl group) R², R³, R⁴ and R⁵ represent optionally substituted phenyl, pyridyl or naphthyl.

10 19. A compound as claimed in Claim 18, wherein the other substituents on the benzene ring of the indole represent hydrogen or G¹.

15 20. A compound as claimed in any one of Claims 2 to 19, wherein R⁶ represents hydrogen or C₁₋₃ alkyl group (which latter group is optionally substituted by G²).

20 21. A compound as claimed in any one of Claims 2 to 20, wherein R⁷ represents phenyl or pyridyl (which groups are optionally substituted by one or more substituents selected from B), or C₁₋₄ alkyl, C₂₋₄ alkenyl or C₅₋₁₀ cycloalkyl (which latter three groups are optionally substituted by one or more substituents selected from G²).

25 22. A compound as claimed in any one of Claims 2 to 19, wherein R⁶ and R⁷ are linked to form a 5- to 6-membered ring optionally substituted by =O.

23. A compound as claimed in any one of Claims 2 to 22, wherein R⁸ and R¹³ independently represent C₁₋₃ alkyl or hydrogen.

24. A compound as claimed in any one of Claims 2 to 23, wherein R¹⁰ represents hydrogen, phenyl, tetrazolyl, C₁₋₄ alkyl, C₂₋₄ alkenyl or C₅₋₆ cycloalkyl, which latter five groups are optionally substituted by one or more substituents selected from G³.

5

25. A compound as claimed in any one of Claims 2 to 24, wherein R¹² represents hydrogen, phenyl, pyrrolyl, C₁₋₄ alkyl or C₅₋₁₀ cycloalkyl, which latter four groups are optionally substituted by one or more substituents selected from G³.

10

26. A compound as claimed in any one of Claims 2 to 25, wherein R¹¹ represents hydrogen or C₂₋₄ alkenyl.

15

27. A compound as claimed in any one of Claims 2 to 26, wherein G³ represents halo, -R¹⁵ or -OR¹⁵.

28. A compound as claimed in any one of Claims 2 to 27, wherein R¹⁵ represents hydrogen, C₁₋₃ alkyl or phenyl.

20

29. A compound as claimed in any one of Claim 16 to 21, wherein the optional substituents are selected from halo, -NO₂, cyano, methylenedioxy, C₁₋₆ alkyl (which alkyl group is optionally substituted by one or more substituents selected from a halo group, a phenyl group and OR¹⁹), C₂₋₆ alkenyl, C₃₋₁₀ cycloalkyl (which cycloalkyl group is optionally substituted with C₁₋₆ alkyl), phenyl (which group is optionally substituted with one or more substituents selected from halo and OR¹⁹), a heteroaryl group selected from tetrazolyl and pyrrolyl (which groups are optionally substituted by one or more C₁₋₆ alkyl groups), methylthio, methylsulfinyl, methylsulfonyl, =O, -OR¹⁹, -N(R¹⁹)R²⁰, -C(O)OR¹⁹, -C(O)R¹⁹, -C(O)N(R¹⁹)R²⁰, -S(O)₂N(R¹⁹)R²⁰ and/or -N(R¹⁹)S(O)₂R²¹, wherein R¹⁹ and R²⁰

30

independently represent hydrogen, phenyl, C₁₋₄ alkenyl, C₁₋₆ alkyl (which alkyl group is optionally substituted by one or more fluoro atoms) or a phenyl group and R²¹ represents phenyl or C₁₋₆ alkyl (which alkyl group is optionally substituted by one or more fluoro atoms).

5

30. A compound as defined in any one of Claims 1 to 29, or a pharmaceutically-acceptable salt thereof, for use as a pharmaceutical.

10 31. A pharmaceutical formulation including a compound as defined in any one of Claims 1 to 29, or a pharmaceutically-acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

15 32. The use of a compound as defined in any one of Claims 1 to 29, or a pharmaceutically-acceptable salt thereof, for the manufacture of a medicament for the treatment of a disease in which inhibition of the activity of microsomal prostaglandin E synthase-1 is desired and/or required.

33. A use as claimed in Claim 32, wherein the disease is inflammation.

20 34. A use as claimed in Claim 33 wherein the disease is inflammatory bowel disease, irritable bowel syndrome, migraine, headache, low back pain, fibromyalgia, a myofascial disorder, a viral infection, a bacterial infection, a fungal infection, dysmenorrhea, a burn, a surgical or dental procedure, a malignancy, atherosclerosis, gout, arthritis, osteoarthritis, 25 juvenile arthritis, rheumatoid arthritis, rheumatic fever, ankylosing spondylitis, systemic lupus erythematosus, vasculitis, pancreatitis, nephritis, bursitis, conjunctivitis, iritis, scleritis, uveitis, wound healing, dermatitis, eczema, psoriasis, stroke, diabetes, a neurodegenerative disorder, an autoimmune disease, osteoporosis, asthma, chronic obstructive pulmonary 30 disease, pulmonary fibrosis, an allergic disorder, rhinitis, an ulcer, coronary

heart disease, sarcoidosis or any other disease with an inflammatory component.

35. A method of treatment of a disease in which inhibition of the activity
5 of mPGES-1 is desired and/or required, which method comprises administration of a therapeutically effective amount of a compound as defined in any one of Claims 1 to 29, or a pharmaceutically-acceptable salt thereof, to a patient suffering from, or susceptible to, such a condition.

10 36. A combination product comprising:

(A) a compound as defined in any one of Claims 1 to 29, or a pharmaceutically-acceptable salt thereof; and
(B) another therapeutic agent that is useful in the treatment of inflammation,
wherein each of components (A) and (B) is formulated in admixture with a
15 pharmaceutically-acceptable adjuvant, diluent or carrier.

37. A combination product as claimed in Claim 36 which comprises a pharmaceutical formulation including a compound as defined in any one of Claims 1 to 29, or a pharmaceutically-acceptable salt thereof, another
20 therapeutic agent that is useful in the treatment of inflammation, and a pharmaceutically-acceptable adjuvant, diluent or carrier.

38. A combination product as claimed in Claim 36 which comprises a kit of parts comprising components:

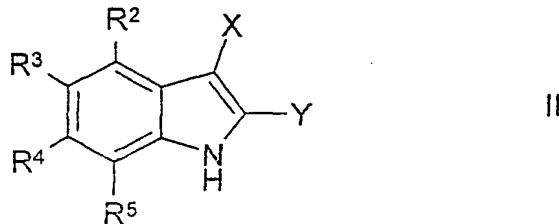
25 (a) a pharmaceutical formulation including a compound as defined in any one of Claims 1 to 29, or a pharmaceutically-acceptable salt thereof, in admixture with a pharmaceutically-acceptable adjuvant, diluent or carrier; and

(b) a pharmaceutical formulation including another therapeutic agent that is useful in the treatment of inflammation in admixture with a pharmaceutically-acceptable adjuvant, diluent or carrier,
 which components (a) and (b) are each provided in a form that is suitable
 5 for administration in conjunction with the other.

39. A process for the preparation of a compound as defined in Claim 2, which comprises:

(i) reaction of a compound of formula II,

10



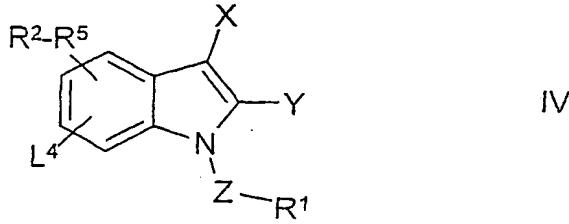
wherein X, Y, R², R³, R⁴ and R⁵ are as defined in Claim 2, with a compound of formula III,

15



wherein L¹ represents a suitable leaving group and R¹ and Z are as defined in Claim 2;

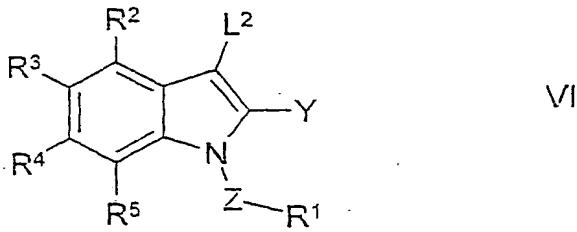
20 (ii) reaction of a compound of formula IV,



wherein L^4 represents L^2 or L^3 , in which L^2 and L^3 represent appropriate leaving groups and L^4 is attached to one or more of the carbon atoms of the benzenoid ring of the indole, and the remaining positions of the benzenoid ring are substituted with 1 to 3 (depending on the number of L^4 substituents) 5 substituents R^2 to R^5 as appropriate, and Z , X , Y , R^1 , R^2 , R^3 , R^4 and R^5 are as defined in Claim 2, with a compound of formula V,



10 wherein R^{22} represents R^2 , R^3 , R^4 or R^5 (as appropriate), and L^5 represents L^2 (when L^4 is L^3) or L^3 (when L^4 is L^2) as defined above;
 (iii) for compounds of formula I in which X represents an optionally substituted aryl or heteroaryl group, reaction of a compound of formula VI,



15

wherein L^2 is as defined above and Z , Y , R^1 , R^2 , R^3 , R^4 and R^5 are as defined in Claim 2, with a compound of formula VII,

20



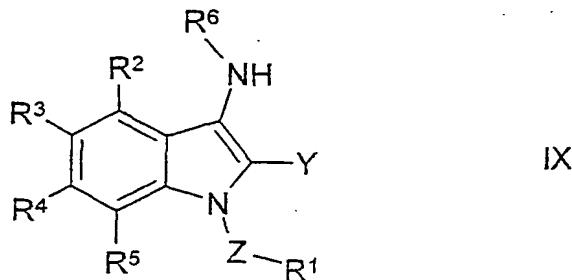
wherein L^3 is as defined above and X^a represents an aryl or heteroaryl group, optionally substituted as defined in Claim 2;

(iv) for compounds of formula I in which X represents $-N(R^6)-E-R^7$, 25 reaction of a compound of formula VI as defined above, with a compound of formula VIII,



wherein E, R⁶ and R⁷ are as defined in Claim 2;

5 (v) for compounds of formula I in which X represents -N(R⁶)-E-R⁷, reaction
of a compound of formula IX,



10 wherein Z, Y, R¹, R², R³, R⁴, R⁵ and R⁶ are as defined in Claim 2, with a compound of formula X,



15 wherein L¹ is as defined above and E and R⁷ are as defined in Claim 2;

(vi) for compounds of formula I in which E represents a single bond and R⁷ is a C₁₋₆ alkyl group, C₃₋₆ alkenyl or a C₃₋₆ alkynyl group, reduction of a compound of formula I, wherein X represents -C(O)- and R⁷ represents H, a C₁₋₅ alkyl group, a C₂₋₅ alkenyl or a C₂₋₅ alkynyl group.